



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 15

[Docket No. FDA-2019-N-1132]

The Future of Insulin Biosimilars: Increasing Access and Facilitating the Efficient Development of Biosimilar and Interchangeable Insulin Products; Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing a public hearing to discuss access to affordable insulin products and issues related to the development and approval of biosimilar and interchangeable insulin products.

DATES: The public hearing will be held on May 13, 2019, from 9 a.m. to 5 p.m. The public hearing may be extended or may end early depending on the level of public participation.

Persons seeking to present at the public hearing must register by April 29, 2019. Persons seeking to speak at the public hearing must register by May 9, 2019. Persons seeking to attend, but not present at, the public hearing must register by May 9, 2019. Section III provides attendance and registration information. Electronic or written comments will be accepted after the public hearing until May 31, 2019.

ADDRESSES: The public hearing will be held at the FDA White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (Rm. 1503B), Silver Spring, MD 20993-0002. Entrance for public hearing participants (non-FDA employees) is through Building 1, where routine security check procedures will be performed. For parking and security

information, please refer to

<https://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm>.

You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before May 31, 2019. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of May 31, 2019. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2019-N-1132 for "The Future of Insulin Biosimilars: Increasing Access and Facilitating the Efficient Development of Insulin Biosimilar and Interchangeable Products; Public Hearing; Request for Comments." Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy,

including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Allison Hoffman, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 32, Rm. 3138, Silver Spring, MD 20993, 301-796-9203, OMPTFeedback@fda.hhs.gov (please use "Insulin Biosimilars part 15" as subject line).

SUPPLEMENTARY INFORMATION:

I. Background

The Biologics Price Competition and Innovation Act of 2009 (BPCI Act) requires that on March 23, 2020, an approved marketing application for a biological product under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355) will be deemed to be a license for the biological product under section 351 of the Public Health Service Act (PHS Act) (42 U.S.C. 262) and regulated under the PHS Act. The transition of biological products currently approved under the FD&C Act to the PHS Act will open the pathway to market for new products that are biosimilar to, or interchangeable with, these transitioned products. The biological products affected by this transition include insulin products, insulin mix products, and insulin analog products (collectively described in this notification as "insulin products"), which historically have been approved under the FD&C Act.

Insulin is a lifesaving drug that many Americans depend on to treat their diabetes. In recent years, however, increases in the prices of insulin products have raised serious concerns about the ability for many patients to access the insulin needed to survive. FDA is holding this public hearing to receive input from stakeholders as the Agency prepares for the submission and review of applications for biosimilar and interchangeable insulin products. FDA anticipates that these products, once they are approved, will bring new competition to the insulin market and help provide affordable treatment options to patients with diabetes without compromising safety and effectiveness.

The BPCI Act amended the PHS Act and other statutes to create an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed biological reference product. This abbreviated pathway allows an applicant to rely on

certain existing knowledge about the safety and effectiveness of a biological reference product to support approval, provided the sponsor can demonstrate that its product meets the applicable statutory standards, including biosimilarity. Thus, the sponsor may be able to develop the biosimilar at a lower cost, relative to the development of a novel biological product submitted in a stand-alone marketing application. The PHS Act defines biosimilarity to mean "that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components" and that "there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product" (section 351(i)(2) of the PHS Act).

An interchangeable biosimilar may be substituted for the reference product without the intervention of the prescribing healthcare provider (see section 351(i)(3) of the PHS Act). To meet the standard of "interchangeability," an applicant must provide sufficient information to demonstrate: (1) biosimilarity; (2) that the biological product can be expected to produce the same clinical result as the reference product in any given patient; and (3) for products administered more than once to an individual, that the risk in terms of safety or diminished efficacy of alternating or switching between the use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch (section 351(k)(4) of the PHS Act).

After the March 23, 2020, transition, insulin products that will be deemed to be licensed under the PHS Act will be able to act as reference products for proposed biosimilar or interchangeable insulin products. There are currently no approved prescription insulin products that can be substituted at the pharmacy level. An interchangeable insulin product can be

substituted for the reference insulin product at the pharmacy, potentially leading to increased access and lower costs for patients.

This public hearing is a component of FDA's broader effort to facilitate the growth of a competitive market for biologics. In July 2018, FDA issued its Biosimilars Action Plan, which focuses on four areas of FDA activities: (1) improving the efficiency of the biosimilar and interchangeable product development and approval process; (2) maximizing scientific and regulatory clarity for the biosimilar product development community; (3) developing effective communications to improve understanding of biosimilars among patients, clinicians, and payors; and (4) supporting market competition by reducing gaming of FDA requirements or other attempts to unfairly delay competition. On September 4, 2018, FDA held a public meeting entitled "Facilitating Competition and Innovation in the Biological Products Marketplace" (see 83 FR 35154, July 25, 2018) and received submissions to an associated docket (Docket No. FDA-2018-N-2689).

II. Purpose and Scope of the Public Hearing

FDA is holding this public hearing to receive input from patients, families, healthcare providers, and other stakeholders who live with diabetes or care for someone with diabetes about the challenges and opportunities FDA should consider as we prepare for the submission and review of applications for biosimilar and interchangeable insulin products. We also want to hear from manufacturers and other stakeholders about the development process for biosimilar and interchangeable insulin products. FDA has determined that a public hearing is the most appropriate way to ensure public engagement on these topics.

Questions for Commenters to Address: FDA is soliciting input on steps the Agency can take to facilitate increased access to insulin products, including biosimilar and interchangeable

insulin products. FDA is interested in how we can encourage the development of biosimilar and interchangeable insulin products, while achieving the balance between competition and innovation intended by Congress in the BPCI Act. Although FDA welcomes all feedback on any public health, scientific, regulatory, or legal considerations relating to this topic, we particularly encourage commenters to consider the following topics and questions as they prepare their comments or statements.

1. Scientific standards for evaluating the biosimilarity and interchangeability of an insulin product.
 - a. What considerations should FDA take into account when evaluating data and other information submitted by an applicant, including from analytical and clinical studies, to determine whether an insulin product is *biosimilar* to a reference product?
 - b. What considerations should FDA take into account when evaluating data and other information submitted by an applicant, to determine whether an insulin product is *interchangeable* with a reference product?
2. Other regulatory considerations: Do certain insulin products, for example, those that include use in insulin pumps for continuous subcutaneous infusion among the approved uses or those approved with over-the-counter marketing status, raise unique scientific considerations? What factors should FDA consider when evaluating a proposed biosimilar or interchangeable insulin product if the reference product raises such considerations? Are there additional factors FDA should evaluate for interchangeable insulin products, which may be substituted at the pharmacy for the reference product without the involvement of the prescriber?

3. Patient experience: What aspects of the patient experience with insulin products should FDA consider when evaluating a proposed biosimilar or interchangeable insulin product?
4. Information resources for patients, clinicians, pharmacists, and other stakeholders: What information is needed to develop effective communications to improve understanding and promote awareness among patients, clinicians, pharmacists, and other stakeholders about biosimilar and interchangeable insulin products?

III. Participating in the Public Hearing

The FDA Conference Center at the White Oak location is a Federal facility with security procedures and limited seating. Attendance will be free and on a first-come, first-served basis. An agenda for the hearing and any other background materials will be made available 5 days before the hearing at

<https://www.fda.gov/FDAgov/NewsEvents/MeetingsConferencesWorkshops/ucm632081.htm>.

If you need special accommodations because of a disability, please contact Allison Hoffman (see FOR FURTHER INFORMATION CONTACT) at least 7 days before the hearing.

Registration and Requests for Formal Oral Presentations: For those interested in presenting at the meeting with a formal oral presentation, please register at <https://www.eventbrite.com/e/insulin-biosimilar-part-15-tickets-56571622245> as "In-person presenter". Presenter registrations are due April 29, 2019.

FDA will try to accommodate all persons who wish to make a formal oral presentation. Formal oral presenters may use an accompanying slide deck. Individuals wishing to present should identify their name, affiliation (if appropriate), and the number of the specific question, or questions, they wish to address. This will help FDA organize the presentations. Individuals and organizations with common interests should consider consolidating or coordinating their

presentations and request time for a joint presentation. Individual organizations are limited to a single presentation slot. FDA will notify registered presenters of their scheduled presentation times. The time allotted for each presentation will depend on the number of individuals who wish to speak. Registered presenters making a formal oral presentation are encouraged to submit an electronic copy of their presentation (PowerPoint or PDF) to OMPTFeedback@fda.hhs.gov with the subject line "Insulin Biosimilars part 15 Presentation" on or before May 6, 2019. Persons registered to present are encouraged to arrive at the hearing room early and check in at the onsite registration table to confirm their designated presentation time. Actual presentation times, however, may vary based on how the meeting progresses in real time.

Registration and Requests for Open Public Hearing Speaker slots: For those interested in participating as an Open Public Hearing speaker, please register at <https://www.eventbrite.com/e/insulin-biosimilar-part-15-tickets-56571622245> as "In-person Open Public Hearing presenter". Open Public Hearing registrations are due May 9, 2019; however, you may sign up as an Open Public Hearing speaker the day of the meeting. Time and space are limited and available on a first-come, first-served basis. Open Public Hearing speakers have less allotted time than formal oral presenters and will deliver oral testimony only (no accompanying slide deck).

Persons registered to participate during the Open Public Hearing are encouraged to arrive at the hearing room early and check in at the onsite registration table to confirm their Open Public Hearing participation.

Those without internet or email access can request to participate as a formal presenter or an open public hearing speaker by contacting Allison Hoffman by the above dates (see FOR FURTHER INFORMATION CONTACT).

In-person attendance: For those who would like to attend in-person, but who are not making a formal presentation or participating in the Open Public Hearing, please register at <https://www.eventbrite.com/e/insulin-biosimilar-part-15-tickets-56571622245> as "In-person attendee--no participation". You may choose not to register; however, seating is limited, and space will be available on a first-come, first-served basis.

Streaming Webcast of the Public Hearing: For those unable to attend in person, FDA will provide a live webcast of the hearing. To join the hearing via the webcast, please go to <https://collaboration.fda.gov/insulin051319>. Please register at <https://www.eventbrite.com/e/insulin-biosimilar-part-15-tickets-56571622245> as "online (webcast only)".

Media: Please register at <https://www.eventbrite.com/e/insulin-biosimilar-part-15-tickets-56571622245> as "Media" by May 9, 2019.

Transcripts: Please be advised that as soon as a transcript is available, it will be accessible at <https://www.fda.gov/FDAgov/NewsEvents/MeetingsConferencesWorkshops/ucm632081.htm> and <https://www.regulations.gov>. It may be viewed at the Dockets Management Staff (see ADDRESSES).

IV. Notice of Hearing Under 21 CFR Part 15

The Commissioner of Food and Drugs is announcing that the public hearing will be held in accordance with part 15 (21 CFR part 15). The hearing will be conducted by a presiding officer, who will be accompanied by FDA senior management from the Office of the Commissioner, the Center for Devices and Radiological Health, the Center for Drug Evaluation and Research, and the Office of the Chief Counsel. Under § 15.30(f) (21 CFR 15.30(f)), the

hearing is informal, and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (21 CFR part 10, subpart C). Under 21 CFR 10.205, representatives of the media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants. Persons attending FDA's hearings are advised that the Agency is not responsible for providing access to electrical outlets. The hearing will be transcribed as stipulated in § 15.30(b) (see *Transcripts*). To the extent that the conditions for the hearing, as described in this notification, conflict with any provisions set out in part 15, this notification acts as a waiver of those provisions as specified in § 15.30(h).

Dated: March 28, 2019.

Lowell J. Schiller,

Acting Associate Commissioner for Policy

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